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searching
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FILE LAST UPDATED: 6 Jun 2008 (20080606/ED)

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=> s SLC and estrone-3-sulfate
2572 SLC
54 SLCS
2603 SLC
(SLC OR SLCS)
16657 ESTRONE
233 ESTRONES
16734 ESTRONE
(ESTRONE OR ESTRONES)
7267544 3
556133 SULFATE
100451 SULFATES
605638 SULFATE
(SULFATE OR SULFATES)
317 ESTRONE-3-SULFATE
(ESTRONE(W)3(W)SULFATE)
L1 3 SLC AND ESTRONE-3-SULFATE

=> d L1 bib abs 1-3

L1 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:656830 CAPLUS
DN 147:109041
TI Scintillation proximity assay for measuring uptake by the human drug transporters hOCT1, hOAT3, and hOATP1B1
AU Lohmann, Christina; Gelius, Birgitta; Danielsson, Jeanette; Skoging-Nyberg, Ulrica; Hollnack, Evelyn; Dudley, Adam; Wahlberg, Johanna; Hoogstraate, Janet; Gustavsson, Lena
CS Discovery DMPK and B, AstraZeneca R&D Lund, Lund, 22187, Swed.
SO Analytical Biochemistry (2007), 366(2), 117-125
CODEN: ANBCA2; ISSN: 0003-2697
PB Elsevier
DT Journal
LA English
AB Increasing evidence suggests a key role of transport proteins in the pharmacokinetics of drugs. Within the solute carrier (SLC) family, various org. cation transporters (OCTs), org. anion transporters

(OATs), and org. anion transporting polypeptides (OATPs) that interact with drug mols. have been identified. Traditionally, cellular uptake assays require multiple steps and provide low exptl. throughput. We here demonstrate the use of a scintillation proximity approach to detect substrate uptake by human drug transporters in real time. HEK293 cells stably transfected with hOCT1, hOATP1B1, or hOAT3 were grown directly in Cytostar-T scintillating microplates. Confluent cell monolayers were incubated with 14C- or 3H-labeled transporter substrates. Cellular uptake brings the radioisotopes into proximity with the scintillation plate base. The resulting light emission signals were recorded online in a microplate scintillation counter. Results show time- and concn.-dependent uptake of 14C-tetraethylammonium, 3H-methylphenylpyridinium (HEK-hOCT1), 3H-estradiol-17.beta.--glucuronide (HEK-hOATP1B1), and 3H-estrone -3-sulfate (HEK-hOAT3), while no resp. uptake was detected in empty vector-transfected cells. Km of 14C-tetraethylammonium and 3H-estrone-3-sulfate uptake and hOAT3 inhibition by ibuprofen and furosemide were similar to conventional dish uptake studies. The scintillation proximity approach is high throughput, amenable to automation and allows for identification of SLC transporter substrates and inhibitors in a convenient and reliable fashion, suggesting its broad applicability in drug discovery.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:65572 CAPLUS

DN 146:288646

TI Organic anion transporting polypeptide 2B1 and breast cancer resistance protein interact in the transepithelial transport of steroid sulfates in human placenta

AU Grube, Markus; Reuther, Sebastian; dMeyer zu Schwabedissen, Henriette; Koeck, Kathleen; Draber, Katrin; Ritter, Christoph A.; Fusch, Christoph; Jedlitschky, Gabriele; Kroemer, Heyo K.

CS Research Center of Pharmacology and Experimental Therapeutics, Department of Pharmacology, Ernst-Moritz-Arndt-University, Greifswald, Germany

SO Drug Metabolism and Disposition (2007), 35(1), 30-35
CODEN: DMDSAI; ISSN: 0090-9556

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AB The human placenta has both protective and nurturing functions for the fetal organism. Uptake and elimination of xenobiotics and endogenous substances are facilitated by various transport proteins from the solute carrier (SLC) and ABC families, resp. A functional interaction of uptake and elimination, which is a prerequisite for vectorial transport

across cellular barriers, has not been described for placenta. In this study, we examd. expression of org. anion transporter (OAT) 4 (SLC22A11), org. anion transporting polypeptide (OATP) 2B1 (SLCO2B1, OATP-B), and breast cancer resistance protein (BCRP) (ABCG2) in human placenta (n = 71) because all three proteins are involved in transmembranal transfer of estrone 3 sulfate (E3S; metabolic product) and dehydroepiandrosterone sulfate (DHEAS; precursor mol.). On the mRNA level, we found a significant correlation of OATP2B1 and BCRP ($R2 = 0.534$; $p < 0.01$) but not between OAT4 and BCRP ($R2 = -0.104$; $p > 0.05$). Localization studies confirmed basal expression of OATP2B1 and apical expression of BCRP. To study functional interactions between OATP2B1 and BCRP, we developed a Madin-Darby canine kidney cell model expressing both transport proteins simultaneously (OATP2B1 and BCRP in the basal and apical membrane, resp.). Using this cell model in a transwell system resulted in a significantly increased basal to apical transport of both E3S and DHEAS, when both transporters were expressed with no change of transfer in the apical to basal direction. Taken together, these data show the potential for a functional interaction of OATP2B1 and BCRP in transepithelial transport of steroid sulfates in human placenta.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:257350 CAPLUS

DN 141:101775

TI Molecular cloning and functional characterization of the bovine (Bos taurus) organic anion transporting polypeptide Oatp1a2 (Slco1a2)

AU Geyer, Joachim; Doring, Barbara; Failing, Klaus; Petzinger, Ernst

CS Institute of Pharmacology and Toxicology, Justus-Liebig-University of Giessen, Giessen, D-35392, Germany

SO Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology (2004), 137B(3), 317-329
CODEN: CBPBB8; ISSN: 1096-4959

PB Elsevier

DT Journal

LA English

AB We describe the cloning, functional characterization and tissue localization of a novel membrane transporter of the OATP/Oatp-gene family obtained from liver and kidney of cattle (Bos taurus). The carrier protein exhibits highest sequence identity to the human OATP1A2 (previously called OATP-A) and is, therefore, named bovine Oatp1a2. Bovine Oatp1a2 received the gene symbol Slco1a2 that is identical to the SLC classification of human OATP1A2 (SLCO1A2, previously called SLC21A3) and is likely an orthologue of the human gene. Two different full-length bOatp1a2 cDNAs of 2316-bp and 3504-bp were obtained and

encoded for a 666 amino acid membrane protein, which contains twelve putative transmembrane spanning domains. Bovine Oatp1a2 expression was detected in liver, kidney, brain and adrenal gland. Uptake studies in cRNA-injected oocytes demonstrated that bOatp1a2 transports estrone-3-sulfate and taurocholate, with Km values of 9.6 .mu.M and 51 .mu.M, resp., and estradiol-17.beta.-glucuronide. However, the structurally-related heart glycosides ouabain (1 .mu.M) and digoxin (1 .mu.M) are neither transported by bovine Oatp1a2 nor by human OATP1A2. We conclude that based on the tested substrates bovine Oatp1a2 shows functional homol. to human OATP1A2.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s estrone-3-sulfate and (breast or mammary)

16657 ESTRONE
233 ESTRONES
16734 ESTRONE
(ESTRONE OR ESTRONES)
7267544 3
556133 SULFATE
100451 SULFATES
605638 SULFATE
(SULFATE OR SULFATES)
317 ESTRONE-3-SULFATE
(ESTRONE(W)3(W)SULFATE)
86916 BREAST
732 BREASTS
87143 BREAST
(BREAST OR BREASTS)
102410 MAMMARY
18 MAMMARIES
102416 MAMMARY
(MAMMARY OR MAMMARIES)

L2 50 ESTRONE-3-SULFATE AND (BREAST OR MAMMARY)

=> s L2 and transport

787052 TRANSPORT
6766 TRANSPORTS
789804 TRANSPORT
(TRANSPORT OR TRANSPORTS)

L3 23 L2 AND TRANSPORT

=> s L3 and (cancer or tumor ot tumour or carcinoma or malignancy)

361761 CANCER

53214 CANCERS
375146 CANCER
(CANCER OR CANCERS)
454333 TUMOR
169801 TUMORS
506652 TUMOR
(TUMOR OR TUMORS)
11220 OT
1570 OTS
12748 OT
(OT OR OTS)
3758 TUMOUR
1424 TUMOURS
5093 TUMOUR
(TUMOUR OR TUMOURS)
0 TUMOR OT TUMOUR
(TUMOR(W)OT(W)TUMOUR)
182701 CARCINOMA
34813 CARCINOMAS
172 CARCINOMATA
191024 CARCINOMA
(CARCINOMA OR CARCINOMAS OR CARCINOMATA)
18215 MALIGNANCY
18670 MALIGNANCIES
34041 MALIGNANCY
(MALIGNANCY OR MALIGNANCIES)
L4 21 L3 AND (CANCER OR TUMOR OT TUMOUR OR CARCINOMA OR MALIGNANCY)

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L5 21 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)

=> d L5 bib abs 1-21

L5 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:255700 CAPLUS
DN 148:302874
TI Method for determining transport activity of a transport protein using scintillation proximity assay technology and membrane vesicles harboring a C-terminus exposed protein
IN Cui, Yunhai
PA Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SO PCT Int. Appl., 36pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2008022956	A1	20080228	WO 2007-EP58473	20070815

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1892530	A1	20080227	EP 2006-119511	20060825

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

PRAI EP 2006-119511 A 20060825

AB A single-tube method is provided which allows a fast and waste-sparing method for detg. transport activity of a transport protein and which addnl. is suitable in high-throughput screening (HTS) as well as in ultra-HTS campaigns for the identification of compds. which can modulate transport activity. A basis for the present invention is the finding that a very C-terminal (i.e., 1 up to 25 amino acids) of a transport protein can be markers (e.g., with a histidine tag) and/or targeted (e.g., with an antibody or antibody fragment) without rendering its transport activity. Thereby, the C-terminus can be used as an anchor in an assay for detg. the activity of the transport protein. A further basis is the well known homogeneous and generic assay technol. called scintillation proximity assay (SPA) technol. Thus, membrane vesicles harboring a transport protein with the C-terminus outside and bound to SPA beads is contacted with a radioactively-labeled substrate which is allowed to be transported into the vesicles. Transport activity is measured, by the light emitted by scintillation of the SPA beads.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:1334438 CAPLUS

DN 148:4480
TI Test systems for ABC transporter proteins using cholesterol loaded insect cell membrane
IN Bathori, Gyoergy; Mehn, Dora; Pal, Akos; Krajcsi, Peter; Szente, Lajos; Fenyvesi, Eva; Telbisz, Agnes; Sarkadi, Balazs; Varadi, Andras; Gedey, Szilvia; Glavinas, Hristos; Kis, Emese; Nagy, Tuende; Nemeth, Attila; Molnar, Eva
PA Solvo Biotechnology, Hung.
SO PCT Int. Appl., 56pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007132279	A2	20071122	WO 2007-HU41	20070514
WO 2007132279	A3	20080103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

HU 2006000408	A2	20080228	HU 2006-408	20060512
PRAI HU 2006-408	A	20060512		
HU 2006-754	A	20060927		

AB The invention provides for a novel cholesterol loaded insect cell membrane prepn. having an increased cholesterol level as compared to physiol. cholesterol levels of insect cell membranes or to control insect cell membrane prepns. without cholesterol loading, wherein said cholesterol loaded membrane prepn. comprises an ABC transporter protein having an increased substrate transport activity due to increased cholesterol level of the membrane. The invention also relates to reagent kits comprising the prepns. of the invention. The invention also relates to methods for manufg. said prepns. and methods for measuring any type of activity of the ABC transporters present in the cholesterol loaded membranes as well as studying or testing compds. and interaction of compds. and ABC transporters, in this assay systems. The invention also provides for a test system useful for testing whether ABC transporter proteins can be activated by cholesterol in an insect cell membrane. The

transport of drugs and other compds. by the ABCG2 and BSEP transporters and interaction of compds. was detd.

L5 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:1199713 CAPLUS
DN 148:51353
TI Human liver-specific organic anion transporter-2 is a potent prognostic factor for human breast carcinoma
AU Muto, Mitsuhisa; Onogawa, Tohru; Suzuki, Takashi; Ishida, Takanori; Rikiyama, Toshiki; Katayose, Yu; Ohuchi, Noriaki; Sasano, Hironobu; Abe, Takaaki; Unno, Michiaki
CS Divisions of Gastroenterological Surgery, Tohoku University Graduate School of Medicine, Sendai, 980-8574, Japan
SO Cancer Science (2007), 98(10), 1570-1576
CODEN: CSACCM; ISSN: 1347-9032
PB Blackwell Publishing Asia Pty Ltd.
DT Journal
LA English
AB Human liver-specific org. anion transporter-2 (LST-2/OATP8/SLCO1B3) was demonstrated to be expressed in various gastrointestinal carcinomas and also to play pivotal roles in the uptake of a wide variety of both endogenous and exogenous anionic compds., including bile acids, conjugated steroids and hormones, into hepatocytes in the human liver. However, the biol. significance of LST-2 in human carcinomas remains unknown. In the present study, the authors examd. the expression of LST-2 in 102 cases of breast carcinoma using immunohistochem. and correlated the findings with various clinicopathol. parameters to examine the possible biol. and clin. significance of LST-2. LST-2 immunoreactivity was detected in 51 cases (50.0%); of these 51 pos. cases, LST-2 immunoreactivity was inversely correlated with tumor size (P = 0.0289). In addn., LST-2 immunoreactivity was significantly assocd. with a decreased risk of recurrence and improved prognosis by both univariate (P = 0.02 and P = 0.01) and multivariate (P = 0.03 and P = 0.01) analyses. In the estrogen receptor-pos. groups, the LST-2-pos. patients showed good prognoses. Considering that LST-2 transports estrone-3-sulfate, these results suggest that LST-2 overexpression is assocd. with a hormone-dependent growth mechanism of the breast cancer . The results of the authors' present study demonstrate that LST-2 immunoreactivity is a potent prognostic factor in human breast cancer.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:976904 CAPLUS
DN 147:314075
TI ABCG2 (breast cancer resistance protein/mitoxantrone resistance-associated protein) ATPase assay: a useful tool to detect drug-transporter interactions
AU Glavinas, Hristos; Kis, Emese; Pal, Akos; Kovacs, Rita; Jani, Marton; Vagi, Erika; Molnar, Eva; Bansaghi, Szava; Kele, Zoltan; Janaky, Tamas; Bathori, Gyorgy; von Richter, Oliver; Koomen, Gerrit-Jan; Krajcsi, Peter
CS SOLVO Biotechnology, Central Hungarian Innovations Center, Budaors, Hung.
SO Drug Metabolism and Disposition (2007), 35(9), 1533-1542
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The ATPase assay using membrane prepns. from recombinant baculovirus-infected Spodoptera frugiperda ovarian (Sf9) cells is widely used to detect the interaction of compds. with different ATP-binding cassette transporters. However, Sf9 membrane prepns. contg. the wild-type ABCG2 transporter show an elevated baseline vanadate-sensitive ATPase activity, which cannot be further stimulated by substrates of ABCG2. Therefore, this assay system cannot be used for the detection of ABCG2 substrates. To overcome this difficulty we (1) purified membranes from a selected human cell line expressing wild-type ABCG2, and (2) inhibited the baseline ATPase activity with different inhibitors. In our modified assay, ABCG2 substrates were able to stimulate the baseline ATPase activity of ABCG2 expressed in membranes of human cells. Furthermore, using the specific ABCG2 inhibitors Ko143 or Ko134 allowed us to suppress the baseline vanadate-sensitive ATPase activity. Substrates of ABCG2 could stimulate this suppressed baseline ATPase, resulting in a better signal-to-background ratio and a robust assay to detect substrates of the ABCG2 transporter. The ATPase assay and the direct vesicular transport measurements for estrone-3-sulfate were in good accordance.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:407458 CAPLUS
DN 146:372197
TI Interactions of cyclosporin A with breast cancer resistance protein
AU Xia, Cindy Q.; Liu, Ning; Miwa, Gerald T.; Gan, Liang-Shang
CS Drug Metabolism and Pharmacokinetics, Drug Safety and Disposition, Millennium Pharmaceuticals, Inc., Cambridge, MA, USA
SO Drug Metabolism and Disposition (2007), 35(4), 576-582

CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The objective of this study was to investigate whether cyclosporin A (CsA) is a modulator for breast cancer resistance protein (BCRP). The interactions between CsA and BCRP were evaluated by using both membrane- and cell-based assays. CsA inhibited BCRP or BCRP R482T mutant-assocd. ATPase with an IC50 of 26.1 and 7.3 .mu.M (31,388 and 8779 ng/mL), resp., indicating that CsA is a modulator for BCRP and its R482T mutant. The apparent permeability (Papp) of CsA was not affected by the BCRP-specific inhibitor Ko143 in both apical-to-basolateral (A-to-B) and basolateral-to-apical (B-to-A) directions in hBCRP- or mBcrp-transfected MDCKII cells, whereas CsA at 50 .mu.M significantly increased the A-to-B transport and decreased B-to-A transport of BCRP substrates, [3H]estrone-3-sulfate ([3H]E3S) and [3H]methotrexate ([3H]MTX), in hBCRP- and mBcrp1-transfected MDCKII cells. Similar to cellular transport studies, CsA did not exhibit ATP-dependent uptake in BCRP-expressed membrane vesicles but inhibited the ATP-mediated E3S and MTX uptake in the same vesicles. The inhibitory const. (Ki) of CsA toward BCRP was 6.7 .mu.M (8507 ng/mL) and 7.8 .mu.M (9380 ng/mL) when using E3S or MTX, resp., as a BCRP substrate. The inhibitory potency of CsA on BCRP wild type or its R482T mutant was lower than that on P-glycoprotein. The present studies demonstrate that CsA is an inhibitor but not a substrate for BCRP, and has low potential to cause drug-drug interactions with BCRP substrate drugs due to its weak inhibitory effect on BCRP and BCRP R482T mutant at its normal therapeutic blood concns. (200-400 ng/mL).
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:65572 CAPLUS
DN 146:288646
TI Organic anion transporting polypeptide 2B1 and breast cancer resistance protein interact in the transepithelial transport of steroid sulfates in human placenta
AU Grube, Markus; Reuther, Sebastian; dMeyer zu Schwabedissen, Henriette; Koeck, Kathleen; Draber, Katrin; Ritter, Christoph A.; Fusch, Christoph; Jedlitschky, Gabriele; Kroemer, Heyo K.
CS Research Center of Pharmacology and Experimental Therapeutics, Department of Pharmacology, Ernst-Moritz-Arndt-University, Greifswald, Germany
SO Drug Metabolism and Disposition (2007), 35(1), 30-35
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics

DT Journal
LA English
AB The human placenta has both protective and nurturing functions for the fetal organism. Uptake and elimination of xenobiotics and endogenous substances are facilitated by various transport proteins from the solute carrier (SLC) and ABC families, resp. A functional interaction of uptake and elimination, which is a prerequisite for vectorial transport across cellular barriers, has not been described for placenta. In this study, we examd. expression of org. anion transporter (OAT) 4 (SLC22A11), org. anion transporting polypeptide (OATP) 2B1 (SLCO2B1, OATP-B), and breast cancer resistance protein (BCRP) (ABCG2) in human placenta (n = 71) because all three proteins are involved in transmembranal transfer of estrone 3 sulfate (E3S; metabolic product) and dehydroepiandrosterone sulfate (DHEAS; precursor mol.). On the mRNA level, we found a significant correlation of OATP2B1 and BCRP ($R2 = 0.534$; $p < 0.01$) but not between OAT4 and BCRP ($R2 = -0.104$; $p > 0.05$). Localization studies confirmed basal expression of OATP2B1 and apical expression of BCRP. To study functional interactions between OATP2B1 and BCRP, we developed a Madin-Darby canine kidney cell model expressing both transport proteins simultaneously (OATP2B1 and BCRP in the basal and apical membrane, resp.). Using this cell model in a transwell system resulted in a significantly increased basal to apical transport of both E3S and DHEAS, when both transporters were expressed with no change of transfer in the apical to basal direction. Taken together, these data show the potential for a functional interaction of OATP2B1 and BCRP in transepithelial transport of steroid sulfates in human placenta.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1123248 CAPLUS
DN 145:449189
TI Inhibitory agent for estrone-3-sulfate transporter activity
IN Tamai, Ikumi; Yabuuchi, Hikaru
PA Genomembrane Co., Ltd., Japan
SO PCT Int. Appl., 30pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2006112330 A1 20061026 WO 2006-JP307751 20060412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
JP 2006298781 A 20061102 JP 2005-119098 20050415
PRAI JP 2005-119098 A 20050415
AB Disclosed is an agent for inhibiting the transporter activity of an estrone-3-sulfate transporter, an agent for inhibiting the growth of breast cancer cells, or an agent for the treatment of breast cancer, which does not need to be incorporated in cells, has excellent drug delivery property and has few side effects. The agent comprises at least one component selected from genistein, quercetin, ginkgolide C, theaflavin, theaflavin 3-o-gallate, chalcone, rutin, daidzein, daidzin, flavanone, flavonol, geraldol, hesperetin, hespereridine, ipriflavone, luteolin-7-o-glucoside, methoxychalcone, 4'-methyl-7-methoxy-isoflavone, 5-morin, myricetin, naringenin, naringenin-7-glycoside, naringin, neohesperidin dihydrochalcone, nomilin, primuletin, poncirin, scutellarein, catechin hydrate, and chem. modified products thereof.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:652528 CAPLUS
DN 145:96426
TI Inhibitors of estrone 3-sulfate transporter and application as the inhibitors for breast cancer cell proliferation and anti-breast cancer drugs
IN Tamai, Ikumi; Nozawa, Takashi; Yabuuchi, Hikaru
PA Geno Membrane K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 26 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

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PI JP 2006176427 A 20060706 JP 2004-370290 20041221
PRAI JP 2004-370290 20041221
AB The inhibitor mixts. for estrone 3-sulfate transporter activity contg. bromosulfophthalein (BSP) as a major component and .gtoreq.1 component selected from , dehydroepiandrosterone sulfate, dehydroepiandrosterone, taurocholic acid, p-aminohippuric acid, tetraethylammonium, probenecid, and benzylpenicillin as active ingredients have been developed. BSP (at 30 and 100 .mu.M) inhibited the estrone 3-sulfate-dependent proliferation of human breast cancer MCF-7 cells (ATCC-HTB22). The inhibitor mixts. can be used as anti-breast cancer drugs.

L5 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:429496 CAPLUS
DN 144:485144
TI Lack of Interaction between Tauroursodeoxycholate and ATP-Binding Cassette Transporter Isoform G2 (ABCG2)
AU Vaidya, Soniya S.; Gerk, Phillip M.
CS Department of Pharmaceutics, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA, 23298, USA
SO Molecular Pharmaceutics (2006), 3(3), 303-306
CODEN: MPOHBP; ISSN: 1543-8384
PB American Chemical Society
DT Journal
LA English
AB Ursodiol (UDCA) is useful for treating several cholestatic hepatic maladies, including intrahepatic cholestasis of pregnancy. Its taurine amidate (TUDC), which accumulates in the bile salt pool, could interact with ABCG2 (ATP-binding cassette transporter isoform G2), which is expressed in various tissues including the canalicular membrane of the hepatocyte and in the apical membrane of the placental syncytiotrophoblast. The purpose of this study was to det. the interaction between TUDC and ABCG2. ABCG2 was expressed in Sf9 cells, and ABCG2-mediated ATP-dependent transport was detd. in sucrose-fractionated Sf9 membrane vesicles. The transport of estrone 3-sulfate (E1S) into ABCG2-expressing membranes was ATP-dependent and was much greater in membrane vesicles expressing ABCG2 vs. the neg. control (empty virus lacking the ABCG2 coding region). To det. whether TUDC affects ABCG2-mediated ATP-dependent transport of E1S, transport activity in the presence of TUDC (20-500 .mu.M) was measured. No significant changes were obsd. in the ABCG2-mediated ATP-dependent E1S transport. Furthermore, ABCG2-mediated TUDC transport was undetectable. Thus, TUDC does not affect ABCG2-mediated E1S transport and is not an ABCG2

substrate.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1034579 CAPLUS
DN 143:359639
TI Suppression of cell proliferation by inhibition of estrone-3-sulfate transporter in estrogen-dependent breast cancer cells
AU Nozawa, Takashi; Suzuki, Masato; Yabuuchi, Hikaru; Irokawa, Masanori; Tsuji, Akira; Tamai, Ikumi
CS Department of Molecular Biopharmaceutics, Faculty of Pharmaceutical Sciences, Tokyo University of Science, Noda, Chiba, 278-8510, Japan
SO Pharmaceutical Research (2005), 22(10), 1634-1641
CODEN: PHREEB; ISSN: 0724-8741
PB Springer Science+Business Media, Inc.
DT Journal
LA English
AB The aim of the study is to suppress the progress of estrogen-dependent breast cancer by inhibiting the membrane transporter, which mediates the internalization of estrone-3-sulfate as estrogen precursor in the cancer cells. The uptake of estrone-3-sulfate by estrogen-dependent breast cancer MCF-7 cells was measured, and inhibitory study using various org. anions on estrone-3-sulfate uptake by MCF-7 cells was conducted. The effects of the inhibitor on the transcription of reporter gene and cell proliferation induced by estrone-3-sulfate were examd. The uptake of estrone-3-sulfate by MCF-7 cells was saturable with Km value of 2.32 .mu.M. The uptake was Na+-independent and was inhibited by several anionic compds. such as bromosulfophthalein. Bromosulfophthalein also significantly inhibited the transcription of reporter gene via estrogen response element and cell proliferation induced by estrone-3-sulfate. However, the transcriptional activation or cell proliferation induced by estrone was not inhibited by bromosulfophthalein. Reverse transcription-polymerase chain reaction anal. revealed the expression of mRNA of org. anion transporting polypeptide (OATP)-D and OATP-E as possible candidates to transport estrone-3-sulfate. The uptake of estrone-3-sulfate is mediated by Na+-independent transporter(s). Inhibitor of estrone-3-sulfate transporter suppressed the transcription and cell proliferation induced by estrone-3-sulfate

in MCF-7 cells. The results provide the basis of a novel strategy for breast cancer treatment by focusing on the transporter responsible for the uptake of estrone-3-sulfate.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:990907 CAPLUS

DN 143:318322

TI Identification of the hepatic efflux transporters of organic anions using double-transfected Madin-Darby canine kidney II cells expressing human organic anion-transporting polypeptide 1B1 (OATP1B1)/multidrug resistance-associated protein 2, OATP1B1/multidrug resistance 1, and OATP1B1/breast cancer resistance protein

AU Matsushima, Soichiro; Maeda, Kazuya; Kondo, Chihiro; Hirano, Masaru; Sasaki, Makoto; Suzuki, Hiroshi; Sugiyama, Yuichi

CS Graduate School of Pharmaceutical Sciences, The University of Tokyo, Bunkyo-ku, Tokyo, Japan

SO Journal of Pharmacology and Experimental Therapeutics (2005), 314(3), 1059-1067
CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AB Until recently, it was generally believed that the transport of various org. anions across the bile canalicular membrane was mainly mediated by multidrug resistance-assocd. protein 2 (MRP2/ABCC2). However, a no. of new reports have shown that some org. anions are also substrates of multidrug resistance 1 (MDR1/ABCB1) and/or breast cancer resistance protein (BCRP/ABCG2), implying MDR1 and BCRP could also be involved in the biliary excretion of org. anions in humans. In the present study, we constructed new double-transfected Madin-Darby canine kidney II (MDCKII) cells expressing org. anion-transporting polypeptide 1B1 (OATP1B1)/MDR1 and OATP1B1/BCRP, and we investigated the transcellular transport of four kinds of org. anions, estradiol-17.beta.-D-glucuronide (EG), estrone-3-sulfate (ES), pravastatin (PRA), and cerivastatin (CER), to identify which efflux transporters mediate the biliary excretion of compds. using double-transfected cells. We obsd. the vectorial transport of EG and ES in all the double transfectants. MRP2 showed the highest efflux clearance of EG among these efflux transporters, whereas BCRP-mediated clearance of ES was the highest in these double transfectants. In addn., two kinds of 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors, CER and PRA, were also substrates of all these

efflux transporters. The rank order of the efflux clearance of PRA mediated by each transporter was the same as that of EG, whereas the contribution of MDR1 to the efflux of CER was relatively greater than for PRA. This exptl. system is very useful for identifying which transporters are involved in the biliary excretion of org. anions that cannot easily penetrate the plasma membrane.

L5 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:424553 CAPLUS
DN 143:41311
TI Expression, localization, and functional characteristics of breast cancer resistance protein in Caco-2 cells
AU Xia, Cindy Q.; Liu, Ning; Yang, David; Miwa, Gerald; Gan, Liang-Shang
CS Drug Metabolism and Pharmacokinetics, Millennium Pharmaceuticals, Inc., Cambridge, MA, USA
SO Drug Metabolism and Disposition (2005), 33(5), 637-643
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The function of breast cancer resistance protein (BCRP) and its role in drug absorption, distribution, and elimination has recently been evaluated. The objective of the present study was to examine the expression, localization, and functional characteristics of BCRP in Caco-2 cells, a widely used human intestinal epithelial cell model for investigating intestinal drug absorption. The expression of BCRP in Caco-2 cells was measured by Western blotting using the antibody BXP-21. Localization of BCRP was detd. by an immunofluorescence technique using both antibodies BXP-21 and BXP-34. The drug efflux function of BCRP was evaluated via the epithelial transport of methotrexate (MTX) and estrone-3-sulfate (E3S) across Caco-2 cell monolayers in the presence or absence of the BCRP inhibitors Ko143 or GF120918 (N-(4-[2-(1,2,3,4-tetrahydro-6,7-dimethoxy-2-isoquinolinyl)ethyl]-phenyl)-9,10-dihydro-5-methoxy-9-oxo-4-acridine carboxamide). Results from Western blot assay indicated that Caco-2 cells in the late passage (p56) expressed a higher level of BCRP as compared with the level in the early passages (p33). The total amt. of BCRP protein did not change after the cells were confluent. Immunofluorescence studies revealed the pos. staining of BCRP on the apical membrane of Caco-2 cells but not on the basolateral membrane after cell confluence. MTX and E3S showed a preferential basolateral-to-apical (B-to-A) transport across Caco-2 cell monolayers. Both BCRP inhibitors Ko143 and GF120918 increased the apical-to-basolateral (A-to-B) transport but decreased the B-to-A transport of MTX and E3S. Caco-2 cells may therefore be used as an in vitro model to study the transport characteristics of BCRP.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:537945 CAPLUS
DN 143:70898
TI Role of the breast cancer resistance protein (ABCG2) in drug transport
AU Mao, Qingcheng; Unadkat, Jashvant D.
CS Department of Pharmaceutics, School of Pharmacy, University of Washington, Seattle, WA, 98195, USA
SO AAPS Journal (2005), 7(1), E118-E133
CODEN: AJAOB6; ISSN: 1550-7416
URL: http://www.aapsj.org/articles/aapsj0701/aapsj070112/aapsj070112.pdf
PB American Association of Pharmaceutical Scientists
DT Journal; General Review; (online computer file)
LA English
AB A review. The 72-kDa breast cancer resistance protein (BCRP) is the second member of the subfamily G of the human ATP binding cassette (ABC) transporter superfamily and thus also designated as ABCG2. Unlike P-glycoprotein and MRP1, which are arranged in 2 repeated halves, BCRP is a half-transporter consisting of only 1 nucleotide binding domain followed by 1 membrane-spanning domain. Current exptl. evidence suggests that BCRP may function as a homodimer or homotetramer. Overexpression of BCRP is assocd. with high levels of resistance to a variety of anticancer agents, including anthracyclines, mitoxantrone, and the camptothecins, by enhancing drug efflux. BCRP expression has been detected in a large no. of hematol. malignancies and solid tumors, indicating that this transporter may play an important role in clin. drug resistance of cancers. In addn. to its role to confer resistance against chemotherapeutic agents, BCRP actively transports structurally diverse org. mols., conjugated or unconjugated, such as estrone-3-sulfate, 17.beta.-estradiol 17-(.beta.-D-glucuronide), and methotrexate. BCRP is highly expressed in the placental syncytiotrophoblasts, in the apical membrane of the epithelium in the small intestine, in the liver canalicular membrane, and at the luminal surface of the endothelial cells of human brain microvessels. This strategic and substantial tissue localization indicates that BCRP also plays an important role in absorption, distribution, and elimination of drugs that are BCRP substrates. This review summarizes current knowledge of BCRP and its relevance to multidrug resistance and drug disposition.
RE.CNT 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:861947 CAPLUS
DN 142:215577
TI Functional analysis of SNPs variants of BCRP/ABCG2
AU Kondo, Chihiro; Suzuki, Hiroshi; Itoda, Masaya; Ozawa, Shogo; Sawada, Jun-ichi; Kobayashi, Daisuke; Ieiri, Ichiro; Mine, Kazunori; Ohtsubo, Kenji; Sugiyama, Yuichi
CS School of Pharmaceutical Sciences, The University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
SO Pharmaceutical Research (2004), 21(10), 1895-1903
CODEN: PHREEB; ISSN: 0724-8741
PB Springer Science+Business Media, Inc.
DT Journal
LA English
AB The aim of the current study was to identify the effect of single nucleotide polymorphisms (SNPs) in breast cancer resistance protein (BCRP/ABCG2) on its localization, expression level, and transport activity. The cellular localization was identified using the wild type and seven different SNP variants of BCRP (V12M, Q141K, A149P, R163K, Q166E, P269S, and S441N BCRP) after transfection of their cDNAs in plasmid vector to LLC-PK1 cells. Their expression levels and transport activities were detd. using the membrane vesicles from HEK293 cells infected with the recombinant adenoviruses contg. these kinds of BCRP cDNAs. Wild type and six different SNP variants of BCRP other than S441N BCRP were expressed on the apical membrane, whereas S441N BCRP showed intracellular localization. The expression levels of Q141K and S441N BCRP proteins were significantly lower compared with the wild type and the other five variants. Furthermore, the transport activity of E1S, DHEAS, MTX, and PAH normalized by the expression level of BCRP protein was almost the same for the wild type, V12M, Q141K, A149P, R163K, Q166E, and P269S BCRP. These results suggest that Q141K SNPs may assoc. with a lower expression level, and S441N SNPs may affect both the expression level and cellular localization. It is possible that subjects with these polymorphisms may have lower expression level of BCRP protein and, consequently, a reduced ability to export these substrates.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:752061 CAPLUS
DN 141:307179
TI Gefitinib reverses breast cancer resistance protein-mediated drug resistance
AU Yanase, Kae; Tsukahara, Satomi; Asada, Sakiyo; Ishikawa, Etsuko; Imai, Yasuo; Sugimoto, Yoshikazu

CS Division of Molecular Biotherapy, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research and Department of Chemotherapy, Kyoritsu University of Pharmacy, Tokyo, Japan
SO Molecular Cancer Therapeutics (2004), 3(9), 1119-1125
CODEN: MCTOCF; ISSN: 1535-7163
PB American Association for Cancer Research
DT Journal
LA English
AB Breast cancer resistance protein (BCRP) is an ATP binding cassette transporter that confers resistance to a series of anticancer agents such as 7-ethyl-10-hydroxycamptothecin (SN-38), topotecan, and mitoxantrone. In this study, we evaluated the possible interaction of gefitinib, a selective epidermal growth factor receptor tyrosine kinase inhibitor, with BCRP. BCRP-transduced human epidermoid carcinoma A431 (A431/BCRP) cells acquired cellular resistance to gefitinib, suggesting that BCRP could be one of the determinants of gefitinib sensitivity in a certain sort of cells. Next, the effect of gefitinib on BCRP-mediated drug resistance was examd. Gefitinib reversed SN-38 resistance in BCRP-transduced human myelogenous leukemia K562 (K562/BCRP) or BCRP-transduced murine lymphocytic leukemia P388 (P388/BCRP) cells but not in these parental cells. In addn., gefitinib sensitized human colon cancer HT-29 cells, which endogenously express BCRP, to SN-38. Gefitinib increased intracellular accumulation of topotecan in K562/BCRP cells and suppressed ATP-dependent transport of estrone 3-sulfate, a substrate of BCRP, in membrane vesicles from K562/BCRP cells. These results suggest that gefitinib may overcome BCRP-mediated drug resistance by inhibiting the pump function of BCRP. Furthermore, P388/BCRP-transplanted mice treated with combination of irinotecan and gefitinib survived significantly longer than those treated with irinotecan alone or gefitinib alone. In conclusion, gefitinib is shown to interact with BCRP. BCRP expression in a certain sort of cells is supposed to be one of the determinants of gefitinib sensitivity. Gefitinib inhibits the transporter function of BCRP and reverses BCRP-mediated drug resistance both in vitro and in vivo.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:1065635 CAPLUS
DN 142:17254
TI Involvement of estrone-3-sulfate transporters in proliferation of hormone-dependent breast cancer cells
AU Nozawa, Takashi; Suzuki, Masato; Takahashi, Koichi; Yabuuchi, Hikaru;

Maeda, Tomoji; Tsuji, Akira; Tamai, Ikumi

CS Department of Molecular Biopharmaceutics, Faculty of Pharmaceutical Sciences, Tokyo University of Science, Noda, Japan

SO Journal of Pharmacology and Experimental Therapeutics (2004), 311(3), 1032-1037
CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AB Although circulating estrone-3-sulfate is a major precursor of biol. active estrogen, permeation across the plasma membrane is unlikely to occur by diffusion because of the high hydrophilicity of the mol. The object of this study was to clarify the involvement of specific transporter(s) in the supply of estrone-3-sulfate to human breast cancer -derived T-47D cells, which grow in an estrogen-dependent manner. The proliferation of T-47D cells was increased by the addn. of estrone -3-sulfate, or estradiol, to the cultivation medium. The initial uptake rate of estrone-3-sulfate kinetically exhibited a single saturable component, with Km and Vmax values of 7.6 .mu.M and 172 pmol/mg of protein/min, resp. The replacement of extracellular Na+ with Li+, K+, or N-methylglucamine+ had no effect on the uptake of [3H]estrone-3-sulfate. The uptake was strongly inhibited by sulfate conjugates of steroid hormones, but not by estradiol-17.beta.-glucuronide. Taurocholate and sulfobromophthalein inhibited the uptake, whereas other tested anionic and cationic compds. did not. The expression of org. anion transporting polypeptides, OATP-D and OATP-E, which are candidate transporters of estrone-3-sulfate, was detected by reverse transcription-polymerase chain reaction anal., although their actual involvement in the uptake of estrogen remains to be clarified. In conclusion, the uptake of estrone-3-sulfate by T-47D cells was mediated by a carrier-mediated transport mechanism, suggesting that the estrogen precursor is actively imported by estrogen-dependent breast cancer cells.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:542898 CAPLUS

DN 141:224038

TI Functional expression of the human breast cancer resistance protein in Pichia pastoris

AU Mao, Qingcheng; Conseil, Gwenaelle; Gupta, Anshul; Cole, Susan P. C.; Unadkat, Jashvant D.

CS Department of Pharmaceutics, School of Pharmacy, University of Washington, Seattle, WA, 98195, USA
SO Biochemical and Biophysical Research Communications (2004), 320(3), 730-737
CODEN: BBRCA9; ISSN: 0006-291X
PB Elsevier Science
DT Journal
LA English
AB We report functional expression of BCRP in Pichia pastoris in which BCRP was produced as a 62 kDa underglycosylated protein. BCRP expression level in P. pastoris was comparable to that in HEK cells. The basal BCRP ATPase activity in the yeast membranes was approx. 40-80 nmol Pi/min/mg protein, which can be modulated by known BCRP substrates and inhibitors. Photolabeling of BCRP with 8-azido[.alpha.-32P]ATP was dependent preferentially on the presence of Co2+ than Mg2+ and could be inhibited by a molar excess of ATP. Vanadate-induced trapping of 8-azido[.alpha.-32P]ADP by BCRP was much more significant in the presence of Co2+ than that with Mg2+. The Km and Vmax values of BCRP for [3H]E1S transport were 3.6 .+-. 0.3 .mu.M and 55.2 .+-. 1.6 pmol/min/mg protein, resp. This efficient and cost-effective expression system should facilitate large scale prodn. and purifn. of BCRP for further structural and functional analyses.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:459152 CAPLUS
DN 139:192696
TI ABCG2 Transports Sulfated Conjugates of Steroids and Xenobiotics
AU Suzuki, Michiko; Suzuki, Hiroshi; Sugimoto, Yoshikazu; Sugiyama, Yuichi
CS School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan
SO Journal of Biological Chemistry (2003), 278(25), 22644-22649
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The mechanism for the cellular extrusion of sulfated conjugates is still unknown. In the present study, we investigated whether human wild type ABCG2 transports estrone 3-sulfate (E1S) using membrane vesicles from cDNA-transfected mouse lymphoma cell line (P388 cells). The uptake of [3H]E1S into ABCG2-expressing membrane vesicles was stimulated by ATP, and the Km value for [3H]E1S was detd. to be 16.6 .mu.M. The ABCG2-mediated transport of [3H]E1S was potently inhibited by SN-38 and many sulfate conjugates but not by

glucuronide and glutathione conjugates or other anionic compds. Other sulfate conjugates such as [3H]dehydroepiandrosterone sulfate (DHEAS) and [35S]4-methylumbelliferone sulfate (Km = 12.9 .mu.M) and [35S]6-hydroxy-5,7-dimethyl-2-methylamino-4-(3-pyridylmethyl)benzothiazole (E3040) sulfate (Km = 26.9 .mu.M) were also transported by ABCG2. Although [3H]methotrexate, [3H]17.beta.-estradiol-17.beta.-D-glucuronide, [3H]2,4-dinitrophenyl-S-glutathione, and [14C]4-methylumbelliferone glucuronide were transported by ABCG2, this took place to a much lesser extent compared with [3H]E1S. It was suggested that ABCG2 preferentially transports sulfate conjugates and that ES and DHEAS are the potential physiol. substrates for this transporter.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:657783 CAPLUS

DN 139:358994

TI Identification of steroid sulfate transport processes in the human mammary gland

AU Pizzagalli, F.; Varga, Z.; Huber, R. D.; Folkers, G.; Meier, P. J.; St-Pierre, M. V.

CS Division of Clinical Pharmacology and Toxicology, Department of Internal Medicine, University Hospital of Zuerich, Zurich, 8091, Switz.

SO Journal of Clinical Endocrinology and Metabolism (2003), 88(8), 3902-3912 CODEN: JCEMAZ; ISSN: 0021-972X

PB Endocrine Society

DT Journal

LA English

AB Circulating hormones and local biotransformation of steroid precursors are both sources of estrogen in human mammary tissue. Estrone-3-sulfate (E1S) is an important estrogenic form in premenopausal women, and dehydroepiandrosterone sulfate (DHEAS) constitutes a major adrenal precursor. Membrane transport systems that govern delivery of these anionic steroid conjugates to the mammary gland were investigated. RNA was screened by RT-PCR and Northern blotting for expression of org. anion transporting polypeptide (OATP) (solute carrier family 21A) and org. anion transporter (OAT) (solute carrier family 22A) gene families. OATP-B (SLC21A9) was the major carrier expressed; OATP-D (SLC21A11) and OATP-E (SLC21A12) were less abundant. In normal sections, OATP-B immunolocalized to the myoepithelium that surrounds the ductal epithelial cells. In invasive carcinoma , ductal epithelial cells were pos. OATP-B was characterized in stable transfected Chinese hamster ovary cells. E1S affinity const. (Km) is 5 .mu.mol/L, max. velocity (Vmax) is 777 pmol/mg.cntdot.min and Km for DHEAS is 9 .mu.mol/L, Vmax is 85 pmol/mg.cntdot.min. The prostaglandins (PG) A1

and PGA2 stimulated uptake of E1S and DHEAS by increasing Vmax 2-fold but not changing Km. The effect of PGA was selectively blocked by the lipophilic thiol reagent N-ethylmaleimide but not by the hydrophilic acetamido-4'(iodoacetyl)aminostilbene-2,2'-disulfonic acid, suggesting an interaction between the electrophilic cyclopentenone ring and specific cysteine residues of OATP-B.

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:88107 CAPLUS
DN 139:4099
TI Transport of sulfated conjugates by human breast cancer resistance protein (BCRP/ABCG2)
AU Suzuki, Michiko; Suzuki, Hiroshi; Sugiyama, Yuichi; Sugimoto, Yoshikazu
CS Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan
SO Japanese Pharmacology & Therapeutics (2002), 30(Suppl. 2), S433-S436
CODEN: JPTABU
PB Raifu Saiensu Shuppan K.K.
DT Journal
LA Japanese
AB The uptake of estrone 3-sulfate (E1S) was obsd. in the BCRP protein-contg. membrane vesicles in the presence of ATP. The E1S uptake was not affected in the presence of glutathione conjugates and glucuronate conjugates, but was suppressed in the presence of sulfate conjugates. The BCRP protein-contg. membrane vesicles also taken up org. anions, such as DHEA sulfate and 4-methylumbellliferone sulfate in the presence of ATP and relatively low uptake of MTX, Estradiol-17.beta.-D-glucuronide, and DNP-SG. Apparently, BCRP may be involved in the transport of E1S and other sulfate conjugates.

L5 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:795665 CAPLUS
DN 132:30824
TI Pharmaceutical composition with tumor necrosis factor-.alpha. or other biological response modifier and 2-methoxyestrone-3-O-sulphamate for inhibition of estrone sulphatase and treatment of cancer
IN Reed, Michael John; Potter, Barry Victor Lloyd
PA Sterix Limited, UK
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 14

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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PI WO 9964013 A1 19991216 WO 1999-GB1835 19990610
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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AB The compn. comprises a sulfamate compd., e.g. 2-methoxyestrone-3-O-sulfamate, and a biol. response modifier, e.g., TNF. The compn. is useful for the prevention and/or treatment of cancer.

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